

Environmental Defense comments on gamma-Butyrolactone.txt
(Submitted via Internet 5/30/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucieryg@msn.com and erauckman@charter.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for gamma-Butyrolactone (CAS# 96-48-0).

The test plan and robust summaries were submitted by the gamma-Butyrolactone (BLO) Consortium and were prepared by the Toxicology and Regulatory affairs Group. BLO is synthesized in several different ways and is used in many industrial applications, including the synthesis of herbicides, growth regulators, vitamin B1 and the rubber additive thiobutyric acid. It is also used as a solvent for sun lotions, printing inks, and petroleum solvents and as a nematocide. Based on these applications, there are many pathways for environmental and human exposures. However no information was provided by the sponsor on the extent of those exposures.

Both the test plan and set of robust summaries were complete, well-written and very informative. The elements of the test plan were supported by appropriate descriptions and explanations of the available studies. The sponsor states that existing studies on this substance are adequate to fulfill requirements of the HPV program. We agree with one possible minor exception. The exception is that solubility data are not fully described in the robust summary. We expect that these data are available but they were inadvertently omitted from the robust summary; they should be added. Other comments are as follows:

1. The aquatic toxicity study was not conducted according to GLP but information is provided on ECOSAR predictions, and the experimental values are in good agreement with the predictions, so we agree with the sponsor that no additional studies are needed. The available data indicate that BLO is rapidly biodegraded and it should not accumulate in the environment.
2. The test plan, helpfully, notes that BLO is metabolized to gamma-hydroxybutyrate, which has effects on the central nervous system and can cause narcosis in animals. The other metabolites of BLO are not toxic.
3. BLO was tested in a full-blown NTP cancer study, and found negative in the 2-year bioassay; these data are more than adequate to fulfill requirements for the repeat dose endpoint.
4. Genetic toxicity studies are mostly negative, with the most significant exception being the chromosomal aberration study in CHO cells. However, BLO does not appear to be carcinogenic so concern over this finding is diminished somewhat.
5. Developmental toxicity studies are available which demonstrate that BLO is not teratogenic. However, there are no reproductive toxicity studies available that were conducted according to OECD guidelines. Two other studies indicate that BLO may effect gonadotropin levels and testicular weights. These studies along with complete histological data from the NTP studies are sufficient to fulfill the screening level requirements of the HPV program for the reproductive toxicity endpoint.

Thank you for this opportunity to comment.

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